Operation Everest II: Plasma Lipid and Hormonal Responses

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ABSTRACT

Lipid metabolism is altered by exposure and acclimatization to high altitude. To examine the effect of high altitude on plasma lipid profiles, fasting-AM blood samples were collected from six men (21-31 yrs) at 760 Torr and periodically during a 40-day exposure to decreasing barometric pressure culminating in a final ambient pressure of 282 Torr. Pre-ascent plasma total cholesterol [TC] concentration, 157.7±9.7 mg/dl, decreased by 25% to 118.3±13.5 mg/dl following the 40-day exposure ($p<0.01$). High density lipoprotein [HDL-C] levels decreased 32% from a pre-ascent value of 46.5±5.1 mg/dl to 31.7±4.1 mg/dl ($p<0.001$) with no alteration in the TC:HDL-C weight ratio. Plasma triglyceride [TG] increased twofold during this period from a pre-ascent level of 57.2±10.0 mg/dl to 103.6±17.7 mg/dl ($p<0.01$). There were no significant differences in fasting plasma free fatty acid [FFA] concentrations or [FFA]:albumin molar ratio throughout the study. Fasting plasma insulin levels were increased from a pre-ascent value of 40.8±2.1 pmole/l to 83.3±17.9 pmole/l after 40-days exposure ($p<0.05$). There were no significant changes in glucagon concentration and the insulin:glucagon molar ratio remained unchanged, averaging 0.98±0.14 throughout the study. Plasma norepinephrine was increased 3-fold from a pre-ascent value of 212±23 pg/ml to 630±126 pg/ml upon reaching 280 Torr ($p<0.01$), with no significant changes in plasma epinephrine concentrations. Mean caloric intake decreased 42% from 3136±227 kcal/day to 1789±278 kcal/day, and mean body weights decreased by 8.9±0.8% ($p<0.01$). Increased concentrations of insulin may lead to increased hepatic production of TG-rich lipoproteins. Unlike the lipid profile

associated with weight loss alone, exposure to high altitude resulted in increased [TG], decreased [TC] and [HDL-C]. Therefore, altitude exposure may elicit metabolic changes independent of weight loss and dietary intake.

INTRODUCTION

Lipid metabolism has been shown to be altered with exposure to high altitude (1,2,7,10,18,19,25,40). Weight loss attributable to loss of body fat (2,19) or lean body mass (7) has been reported with long-term exposure to high altitude. Furthermore, exposure to high altitude led to increased (40) circulating triglyceride levels and reduced (10) or unchanged (40) plasma cholesterol concentrations. Thus, the effects of exposure to high altitude on lipid metabolism appear to be complex, interrelated processes involving multiple responses by the body.

Lipid metabolism is a dynamic process involving a highly integrated series of events. In blood, fats are transported in lipoprotein particles that consist of a core of lipid, cholesterol ester or triglyceride, stabilized by an outer layer of protein and phospholipid. Dietary fats are transported as chylomicrons and are not present in fasting plasma of healthy, normolipemic individuals. Endogenously derived plasma lipids are contained in three major lipoprotein classes: very low density lipoprotein (VLDL), a triglyceride-rich lipoprotein synthesized by the liver; and two cholesterol-rich particles, low density lipoprotein (LDL) and high density lipoprotein (HDL). VLDL has been shown to be a direct precursor of LDL and HDL, although nascent HDL can also be secreted directly by the liver (30,39). A perturbation of this intrinsic balance can result accumulation of lipoprotein

particles in the blood that could ultimately result in diseases such as atherosclerosis and the hyperlipoproteinemias.

Since high altitude has been shown to alter lipid metabolism, the fasting lipid profiles and hormonal responses of eight human subjects were determined at sea level and during a 40-day hypobaric chamber study that simulated the ascent to Mt. Everest. The study, entitled Operation Everest II, was unique in that it examined the chronic effects of hypoxia without additional environmental stresses.

MATERIALS AND METHODS

During the course of Operation Everest II, six male test subjects (aged 21-31 yr) were decompressed from sea level (SL, 760 Torr) to 282 torr over a 40-day period. During the last week of the study, the subjects were exposed periodically to 240 Torr for additional testing at the simulated summit of Mt. Everest. Of the initial eight subjects, two subjects were unable to complete the study and their data are not included here. Operation Everest II was conducted in the hypobaric chamber at the U. S. Army Research Institute of Environmental Medicine (USARIEM), in Natick, MA (50 m). Complete details of Operation Everest II were published elsewhere (16). During the study the cycling maximal oxygen uptake ($\dot{V}O_2$ max) of each subject was determined using a discontinuous protocol. Details of the non-invasive instrumentation and measurements taken during exercise are published elsewhere (13).

From the onset of the study at sea level and through the last day in the hypobaric chamber, the subjects consumed an ad libitum diet. The menus, food preparation, and dietary data collection were supervised by a registered dietician and complete details are described elsewhere (29). Briefly, the subjects selected three meals daily from menus consisting of approximately 3000 kcal/day distributed to provide 60% carbohydrate, 15% protein, and 25% fat in the diet. A variety of foods and non-alcoholic beverages were available for snacks. Foods were weighed before and after the meal and intakes were analyzed using the University of Massachusetts Nutrient Data Bank program. Gross fluid balance was determined by subtracting the urine output from the fluid intake. Each morning, the subjects were weighed after arising and voiding.

Before the subjects arose in the morning and while remaining in a supine position, blood samples were obtained following a overnight fast. Blood samples were obtained prior to ascent (day 1), 450 Torr (day 7), 380 Torr (day 14), 335 Torr (day 25), 282 Torr (day 32), 282 Torr (day 40), and less than 24 hours after returning to sea level (day 41). Blood was obtained from an 18-gauge butterfly catheter that was placed in an antecubital vein. The catheter was in place for at least 10-min prior to sampling and kept patent by a 0.9% saline lock containing no heparin. Blood was collected in disodium ethylenediaminotetraacetate (EDTA) and stored on ice. Blood samples were transferred from the chamber to the laboratory through an airlock within 10-min of collection. An aliquot of blood was analyzed for standard hematology with a Coulter Counter (model S880, Hialeah, FL). Blood samples for analysis of glucagon concentration were collected in

ethylene-bis(oxyethylenenitrile)tetraacetic acid (EGTA) with a protease inhibitor, Aprotinin (Sigma Chemical Co., St. Louis, MO).

The blood was centrifuged (4°C), plasma separated, and aliquoted for each assay. For determination of high density lipoprotein cholesterol [HDL-C] concentration, very low density lipoproteins [VLDL] and low density lipoproteins [LDL] were precipitated from plasma by addition of magnesium dextran sulfate (Sigma Chemical Co., St Louis, MO) and removed by centrifugation (22). The supernatant was saved in a separate aliquot for determination of [HDL-C]. Another aliquot of untreated plasma was saved for analysis of total cholesterol [TC] concentration. Plasma aliquots were stored in liquid nitrogen (-196°C) until analyzed. Plasma [HDL-C] and [TC] were determined by an enzymatic method (Sigma Chemical Co., St Louis MO). Plasma insulin concentration was determined using a commercial radioimmunoassay kit (Serono Diagnostics, Braintree, MA). Plasma glycerol and triglyceride concentrations were quantified by enzymatic assay (Behring Diagnostics, La Jolla, CA) as were plasma free fatty acid (FFA) levels (Nippon Shoji Kaisha, Osaka, Japan). Plasma glucose concentrations were determined using an enzymatic autoanalyzer (Beckman, Palo Alto, CA). Plasma catecholamine levels were determined by a HPLC method (9). Plasma albumin concentration was determined by a colorimetric assay (Sigma Chemical Co., St Louis, MO). With each analysis, appropriate standard curves and QC plasma samples were assayed. All samples from each subject were analyzed in triplicate at the same time to avoid interassay variation.

Data were analyzed using a three-way analysis of variance (ANOVA) using a BMDP statistical program (P4V). A Newman-Keuls multiple range critical

difference test was used to identify significant differences between means. Statistical significance was accepted at $p < 0.05$. Unless otherwise stated, data are expressed as Mean±SEM.

RESULTS

Subject fitness, nutritional status, weight loss, and changes in body composition

Maximal $\dot{V}O_2$ uptake. Pre-ascent cycling $\dot{V}O_2$ max averaged 3.95±0.24 l/min. Progressive altitude exposure resulted in marked reductions in $\dot{V}O_2$ max and are reported elsewhere (34). Within 24 hours after returning to sea level, mean cycling $\dot{V}O_2$ max was 3.24±0.16 l/min, an 18% decrease when compared to pre-ascent ($p<0.01$).

Daily caloric consumption. Initially, the subjects consumed 3136±227 kcal/day with 62.1±2.9% (1947±222 kcal/day) of the calories from carbohydrate, 14.3±1.3% (450±97 kcal/day) from protein and 25.1±3.1% (787±235 kcal/day) from fat. Daily caloric intake decreased significantly throughout the altitude sojourn. During the last 3 days of the study, while at a simulated altitude varying between 282-240 Torr, the subjects decreased their caloric intake by 42.3% to 1789±278 kcal/day ($p<0.001$) with 53.2±2.9% (952±127 kcal/day) from carbohydrate, 14.3±2.6% (256±68 kcal/day) from protein, and 33.0±3.2% (590±170 kcal/day) from fat (29). The daily intake of cholesterol was approximately 380 mg/day and did not exceed an average amount of 722±185 mg/day. Initially, the polyunsaturated fat to saturated fat (P:S

ratio) was 0.78±0.44 (mean±SD) and during the final week of exposure the P:S ratio declined to 0.32±0.21 (mean±SD).

Weight loss. The subjects lost an average of 7.4±0.9 kg during the study, representing approximately 8.9±0.8% of their initial body weight. Each subject lost more weight than expected on the basis of calculated energy expenditure and caloric intake (29). Data from hydrostatic weighing and computerized tomography scans indicated that of the weight lost, approximately 33% came from body fat and 67% from lean body mass (LBM) (29). For all subjects, total fluid intake exceeded total urine output, indicating that the subjects were not hypohydrated (29).

Plasma Lipid Concentrations

Plasma Triglyceride, Free Fatty Acid, Glycerol and Glucose Concentrations. Fasting-AM plasma triglyceride [TG] concentrations are shown in Fig 1. At 760 and 450 Torr, plasma [TG] were 57.2±10.0 mg/dl and 66.0±10.6 mg/dl, respectively. At 380 Torr and 335 Torr plasma [TG] was increased approximately 1.5 fold to 93.9±20.8 mg/dl and 95.1±11.0 mg/dl, respectively ($p<0.05$). At 282 Torr, plasma [TG] remained elevated at 103.6±17.7 mg/dl after 24 h exposure and 82.7±8.2 mg/dl after 7 days sojourn at 282 Torr. Plasma samples were obtained from the subjects within 24 hours after their return to sea level. However, diet was not monitored for this 24-hour period and triglyceride values are not reported.

Fasting-AM plasma total cholesterol [TC] and high density lipoprotein cholesterol [HDL-C] concentrations are shown in Fig 2. Pre-ascent plasma

[TC] averaged 157.7±9.7 mg/dl and decreased throughout the study. After 7-days of exposure to 282 Torr, plasma [TC] was 118.3±13.5 mg/dl, representing a 25% decrease when compared to pre-ascent values ($p<0.01$). Although dietary controls were not placed upon the subjects after their return to sea level, plasma [TC], 116±13.7 mg/dl, remained significantly ($p<0.01$) decreased when compared to pre-ascent values. A similar decline in plasma [HDL-C] was observed. Initial, pre-ascent values for [HDL-C] averaged 46.5±5.1 mg/dl. After 7 days at 282 Torr, plasma [HDL-C] was decreased by 30% to 32.7±4.5 mg/dl ($p<0.001$). Upon return to sea level, plasma [HDL-C] remained decreased, 29.8±3.8 mg/dl, when compared to pre-ascent values ($p<0.01$). For the present study the TG:TC weight ratio decreased from 3.1±0.5 at sea level to 1.5±0.2 after 7 days at 282 Torr ($p<0.01$). The TC:HDL-C ratio remained unchanged at 4.04±0.23 throughout the 40-day experimental period.

For normolipemic subjects, an approximation of the amount of cholesterol contained in the VLDL fraction or VLDL-C can be obtained by dividing the total plasma TG concentration by a factor of 5 (31). For the data obtained in this study, the pre-ascent value of VLDL-C is approximately 11.4±2.0 mg/dl and was increased by 82% to 20.7±3.5 mg/dl during the 40-day experimental period ($p<0.01$). Prior to ascent, this calculated value for VLDL-TG represents 7.2% of the TC in plasma and as much as 17.5% of the TC following altitude exposure.

Fasting-AM plasma glycerol, FFA, and FFA:glycerol molar ratio are shown in Table 1. Throughout the 40-day experimental period, fasting-AM plasma free fatty acid (FFA) concentrations were not significantly different, averaging 446±39 uequiv/l. Also, the fasting-AM FFA:albumin molar ratio remained

unchanged at 0.62±0.06, overall for the entire 40-day experimental period. Fasting plasma glycerol concentrations were decreased at altitude when compared to values obtained before ascent ($p<0.05$). During most of the 40-day exposure period the FFA:glycerol molar ratio remained unchanged, but was elevated to 14.5±4.5 during the first 24 h of exposure to 282 Torr ($p<0.05$). Fasting plasma glucose concentrations were unchanged, averaging 4.87±0.05 mM throughout the study.

Plasma Hormone Concentrations

Insulin and Glucagon Concentrations. Prior to ascent, fasting-AM plasma insulin levels (Fig 3) were 40.8±2.1 pmole/l and were not changed at 450 and 380 Torr. However, with ascent to 335 and 282 Torr, plasma insulin levels increased approximately 2-fold to 78.0±9.3 pmole/l and 79.0±13.6 pmole/l, respectively ($p<0.05$). After 7 d sojourn at 282 Torr, plasma insulin levels remained elevated, 83.3±17.9 pmole/ml, when compared to pre-ascent values ($p<0.05$) and remained elevated (98.8±17.2 pmole/l) following return to 760 Torr ($p<0.05$). Throughout the 40-day experimental period, fasting-AM plasma glucagon levels remained constant, averaging 112.6±10.1 pmole/l. The fasting-AM insulin:glucagon molar ratio was unchanged, averaging 0.98±0.14 overall.

Catecholamine Concentrations. During the sea level phase and the ascent to 450, 380 and 335 Torr, fasting-AM plasma norepinephrine [NE] levels (Fig 4) were not increased significantly, but increased 3-fold to 630±127 pg/ml within 24 hours of arrival at 282 Torr ($p<0.01$). After 7 days sojourn at 282 Torr, plasma [NE] was 351±41 pg/ml, a significant decrease when compared

to initial [NE] upon reaching 282 Torr ($t<24h$) ($p<0.05$). Twenty-four hours after returning to 760 Torr plasma [NE] levels were not significantly different from pre-ascent values. Fasting plasma epinephrine concentrations were not changed throughout the 40-day experimental period, averaging 35.7±4.1 pg/ml.

Growth Hormone Concentrations. Fasting-AM plasma growth hormone concentrations were not significantly different during the course of the study, averaging 3.3±0.6 ng/ml.

DISCUSSION

When mountaineers ascend to high altitude, they may encounter not only hypoxia, but cold climate, inadequate food and water supplies, and fatigue from exhausting work (16). Thus, it is difficult to isolate the effects of hypoxia from the other components of the mountainous environment. The goal of Operation Everest II was to simulate the hypoxic stress of high altitude by exposing 8 men to decreased ambient PO_2 while supplying them with an adequate diet in a comfortable setting (16). During the study, the subjects experienced anorexia as seen by their voluntary ingestion of a hypocaloric diet, weight loss, and a decrement in maximal oxygen uptake. Also, fasting plasma TG accumulation was increased with a concurrent decrease in plasma total cholesterol (TC) and HDL-C levels. Along with these changes in plasma lipids, circulating concentrations of insulin and norepinephrine were increased while epinephrine, growth hormone and glucagon levels remained unchanged. Thus, exposure to increased altitude elicited complex physiological and biochemical responses.

Throughout the experimental period the subjects consumed an diet calculated to meet their energy expenditure and nutrient requirements (29). The intake of dietary fat was in accordance with guidance established by the American Heart Association (AHA) recommending restriction of dietary fat intake to less than 30% of the total daily caloric consumption (15). At the higher altitudes, the percentage of kcal from fat was 33%, representing a significant increase over the pre-ascent daily fat caloric consumption of 25% (29). However, since the subjects consumed less total calories at the higher altitudes, the pre-ascent fat consumption was 784 kcal/day, a greater amount than the 590 kcal dietary fat/day at 282 Torr. Therefore, the slight alteration in dietary fat consumed during the study does not appear to be a major factor in the alteration of the plasma TG profile. Additionally, since the relative percentages of carbohydrate consumed remained approximately unchanged throughout the study and the actual amount of carbohydrate consumed decreased, increased consumption of carbohydrate does not appear to have contributed to the increased accumulation of plasma TG.

Dietary manipulation is an important therapy for reduction of plasma lipids, specifically cholesterol (33). Most diets recommend a decreased intake of cholesterol and partial substitution of saturated by polyunsaturated fatty acids (14). Such dietary modification over a six month time period can result in a reduction of plasma TC by as much as 17% (20). Consumption of a diet low in saturated fats and cholesterol over a three month time period caused an decrease in TC of 32mg/dl with no change in TG (33). In the present study, the diet contained a moderate amount of cholesterol varying between approximately 300 and 500 mg/day, slightly more

than the amount recommended for reduction of plasma TC levels. Additionally, for reduction of plasma TC levels, the AHA recommends maintenance of a dietary P:S ratio of approximately 1 (15). In the present study, the subjects voluntarily consumed a diet with a P:S ratio consistently lower than 1 and continued to decrease the P:S ratio in their diet. Thus, the amount of cholesterol consumed in the diet coupled with the steady decrease in the P:S ratio could have resulted in increased plasma TC, rather than the decrease in TC observed in the present study.

Of additional concern would be the voluntary restriction of caloric intake upon reaching the higher altitudes. During actual ascent, mountaineers cite lack of water, environmental conditions and overall fatigue as reasons for limiting caloric intake and food consumption. These were not factors in the present study. The subjects had unlimited access to any type of food they requested. Also, the diets were nutritionally balanced with the goal to stimulate the subject's appetite and meet his caloric needs (29). Yet each subject lost significant amounts of LBM and body fat.

Loss of weight has been reported to decrease fasting blood TG levels. (26). Loss of approximately 11 kg in normal and hypertriglyceridemic individuals resulted in a decrease in plasma TG and TC levels (26). Also, weight loss is prescribed as a treatment of endogenous hypertriglyceridemia (type IV), a genetic disease characterized by elevated VLDL-TG concentration in plasma (26). Thus, weight loss alone can be effective in lowering plasma TG levels. In the present study, the subjects lost a similar amount of weight, 7.4 kg, but had increased plasma TG and decreased TC.

With increasing hypoxic exposure, plasma insulin and norepinephrine concentrations were elevated. High concentrations of plasma insulin lead to decreased rate of FFA release from adipose tissue (6). While increased norepinephrine concentrations increase cyclic AMP levels in adipose in opposition to insulin action (5). Since these hormones were present in increasing amounts throughout the experimental period, it is possible that both norepinephrine and insulin may have exerted their diverse metabolic actions.

Once mobilized, FFA may enter the bloodstream where their efflux is concentration driven (17). Plasma FFA concentration and plasma turnover rate have been positively correlated (17). Further, experiments with cultured rat hepatocytes have shown that increasing the ambient FFA concentration results in increased TG synthesis and release of VLDL-TG (8) Also, plasma insulin levels and VLDL-TG secretion rate have been positively correlated (37). Therefore, it is possible that increased concentrations of circulating norepinephrine resulted in mobilization of FFA. Through insulin action, FFA were taken up by the liver and incorporated into VLDL-TG. Thus, in the present study, a "set point" may have been reached for fasting FFA levels such that any excess accumulation in fasting plasma would result in FFA uptake and increased synthesis of TG by the liver.

Previous studies at lower altitudes have reported diverse effects on plasma lipid profiles (1,10,18,25,40). In the present study, we have demonstrated a significant increase in plasma TG similar to that of Whitten and Janoski during a 9-day altitude study on the summit of Pikes Peak (4300m) (40). However, in that study, plasma TC levels were unchanged and fasting FFA

increased approximately 2-fold (40). Also, there was a significant weight loss of 4.27 kg that the authors assume was solely body fat (40). For the present study, data indicated that the weight loss was predominantly protein (29). In another study, following an 8-week climb between the altitudes of 4,000 and 7,130 m (465 Torr to 310 Torr), the concentration of plasma apolipoprotein A-I, the major protein of HDL, increased 2-fold but, the HDL cholesterol levels were not reported (25). In another short-term exposure to 3800m altitude, plasma TC was increased after 3-weeks (1). Long term residence has also been reported to alter cholesterol levels. Comparison of plasma cholesterol levels in socio-economically matched high (3500m) and lower (1000m) altitude natives of Peru showed that the low altitude residents had higher total cholesterol levels, predominantly LDL-C (10). Although the effects of altitude exposure on blood lipid profile are diverse, this may be the result of varying altitudes, duration of exposure, diet, and exercise.

During altitude studies, test subjects may assume a sedentary lifestyle that results in detraining (41). In the present study, the subjects attempted to maintain a their level of fitness by exercising daily on several types of ergometers (16). However, they detrained during the 40-day experimental period as evidenced by an 18% reduction in $\dot{V}O_2$. While this may have occurred due to the relatively sedentary lifestyle typical of chamber confinement, the loss of approximately 5 kg LBM may have also contributed to their decrement in exercise capacity.

A significant hypolipemic response to exercise training in humans has been described (27), but the mechanism has not been elucidated. After 7-weeks of a light aerobic training program, serum TG, TC decreased and HDL-C

increased (36). Also, distance runners had higher HDL levels than sedentary controls (36). Thus, if exercise training leads to a more healthy lipid profile, the effect of detraining should be investigated. It is possible that the detraining observed in the present study may have contributed to the altered lipid profile.

The increase in fasting TG levels appears to be at the expense of plasma TC and HDL-C accumulation. VLDL is a direct precursor of LDL and a partial contributor to HDL. Lipoprotein lipase (LPL) modulates HDL levels by promoting the hydrolysis of lower density lipoproteins, namely chylomicrons and VLDL, and transfer of lipid to HDL (35). Alternatively, it has been proposed that hepatic lipase activity modulates HDL by regulating its removal (39). Thus, reduced HDL-C concentration may occur through either increased removal by the liver or decreased conversion from TG-rich lipoproteins. Therefore, the liver is pivotal in HDL regulation, either by removing HDL from circulation or by the synthesis of VLDL, whose metabolic fate through the action of LPL is conversion to HDL. In turn, failure of LPL to hydrolyze VLDL-TG could result in increased accumulation of plasma TG and reduction in HDL-C. Weight loss has been shown to increase the activity of LPL in adipose tissue (32). Should this occur with weight loss at altitude, LPL mediated removal of TG-rich lipoproteins should proceed normally or at an enhanced rate.

In the fasting state, the LPL activity of skeletal muscle is inversely related to the insulin:glucagon molar ratio (21). Therefore increased plasma insulin concentration should depress LPL activity. In humans, glucagon excess has been reported to depress TG synthesis by the liver and reduce

plasma TG accumulation (22). Thus, the constant levels of glucagon seen in the fasting blood samples combined with increased insulin levels should result in increased hepatic production of TG-rich lipoproteins (4).

There is considerable evidence of an inverse relationship between the insulin:glucagon molar ratio and the need for endogenous energy production. In the present study, the fasting insulin:glucagon molar ratio was less than 1 and remained unchanged during the 40-day sojourn. This ratio has been reported to be indicative of total starvation or extreme physical exercise (3) and a catabolic metabolic state (38).

This study demonstrates a dynamic alteration in lipid physiology during exposure to extreme hypobaric hypoxia. Upon exposure to high altitude, fasting plasma TG accumulation was increased with a concurrent decrease in plasma TC and HDL-C levels. It is possible that increased insulin concentration resulted in increased TG synthesis by the liver and depressed the mobilization of fatty acids from depot fat. Along with increased levels of plasma TG, an apparent block may occur in the catabolism of the TG-rich lipoproteins to the cholesterol-rich lipoproteins, LDL and HDL. If we consider fasting plasma TG accumulation to be the balance between liver production and peripheral removal, chronic altitude exposure may result in increased production and decreased removal of TG-rich lipoproteins.

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TABLE 1 Effect of altiude exposure on fasting-AM on plasma glycerol, free fatty acid (FFA), and FFA:glycerol molar ratio.

	Plasma Glycerol (uM)	Plasma FFA (uequiv/l)	FFA:Glycerol Molar Ratio
760 Torr	182.6 ±23.8	428.2 ±95.5	2.5 ±0.7
450 Torr	84.9[a] ±17.2	535.2 ±110.4	8.4 ±3.4
380 Torr	82.1[a] ±19.7	634.2 ±126.3	8.2 ±1.2
335 Torr	61.1[a] ±10.8	324.5 ± 46.3	5.5 ±0.5
282 Torr (t<24h)	56.8[a] ±11.3	601.2 ±111.7	14.5[b] ±4.5
282 Torr (t=7d)	49.1[a] ± 8.2	409.7 ± 65.0	9.9 ±2.2

a=p<0.05 from 760 Torr
b=p<0.01 from 760 Torr

Figure Legends

Figure 1: The effect of altitude on fasting plasma triglyceride concentrations.
** = p<0.01 from 760 Torr
* = P<0.05 from 760 Torr

Figure 2: The effect of altitude on fasting total cholesterol and high density lipoprotein (HDL) cholesterol concentrations.
** = p<0.01 from 760 Torr

Figure 3: The effect of altitude on fasting plasma norepinephrine concentrations.
** = p<0.01 from 760 Torr

Figure 4: The effect of altitude on fasting plasma insulin concentrations.
** = p<0.01 from 760 Torr
* = p<0.05 from 760 Torr

FIGURE 1

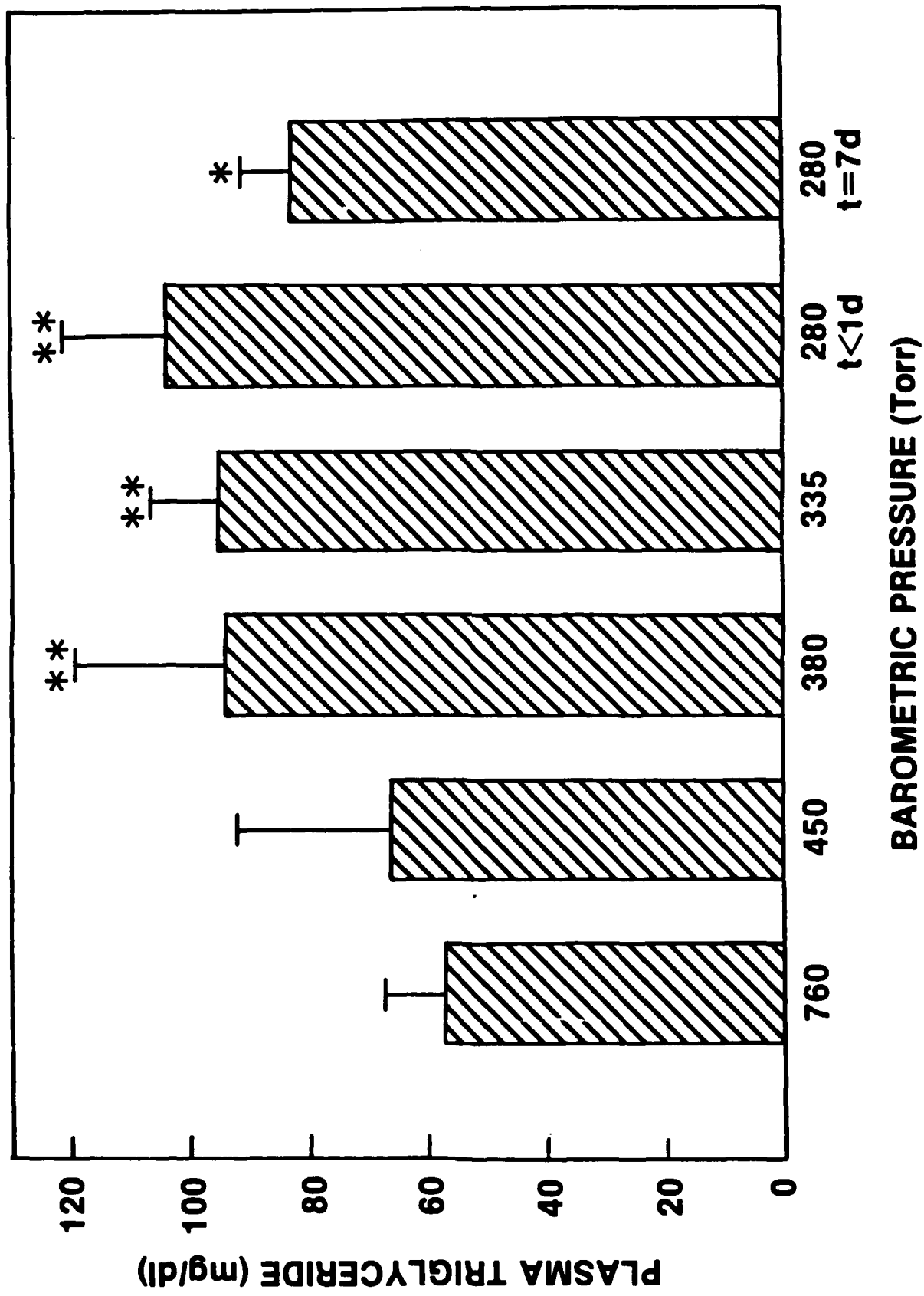

PLASMA TRIGLYCERIDE (mg/dl)
0
20
40
60
80
100
120
760
450
380
335
280 t<1d
280 t=7d
BAROMETRIC PRESSURE (Torr)
*
**
**
**

FIGURE 2

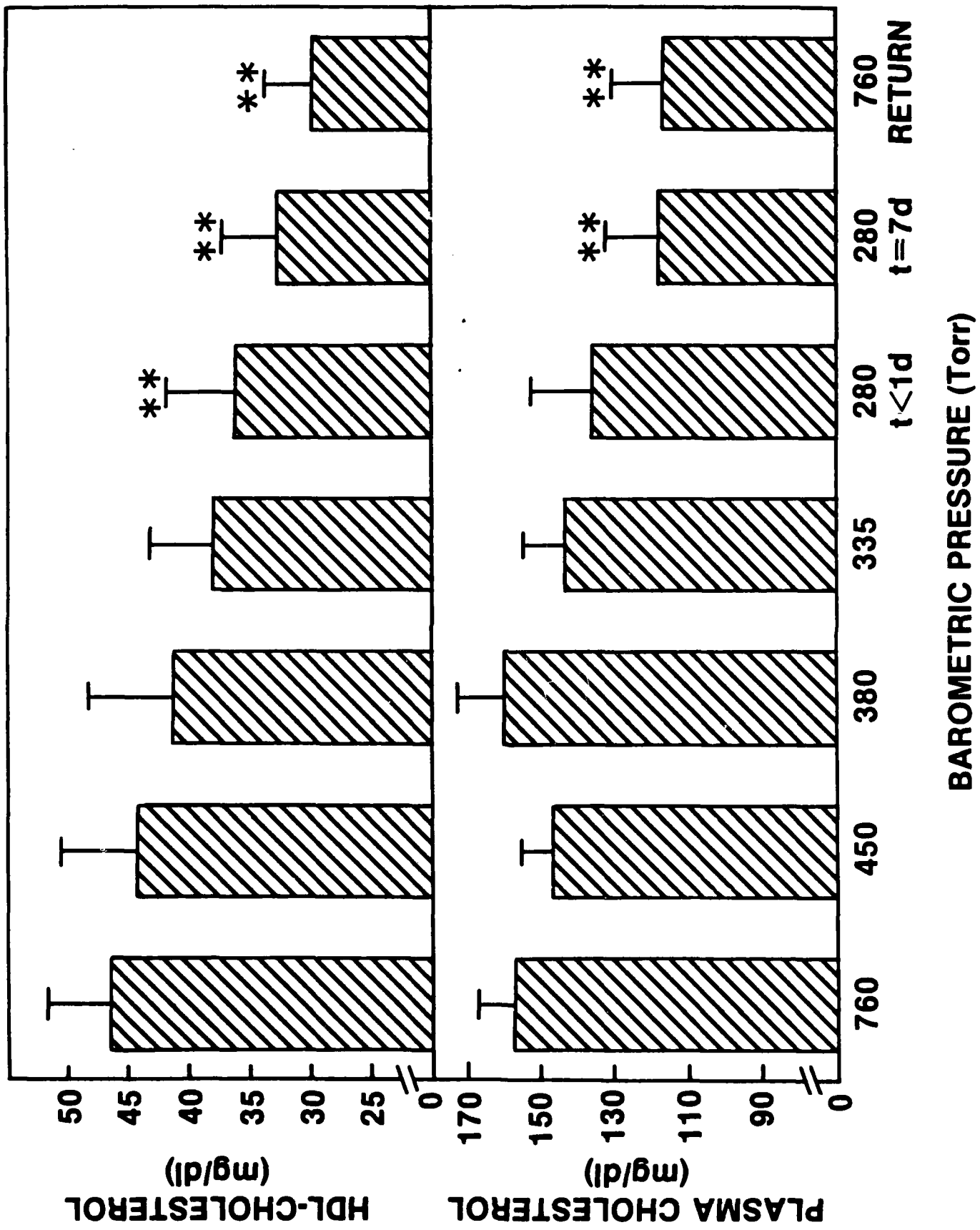

HDL-CHOLESTEROL (mg/dl)
50
45
40
35
30
25
0
PLASMA CHOLESTEROL (mg/dl)
170
150
130
110
90
0
**
**
**
760
450
380
335
280 t<1d
280 t=7d
760 RETURN
BAROMETRIC PRESSURE (Torr)

FIGURE 3

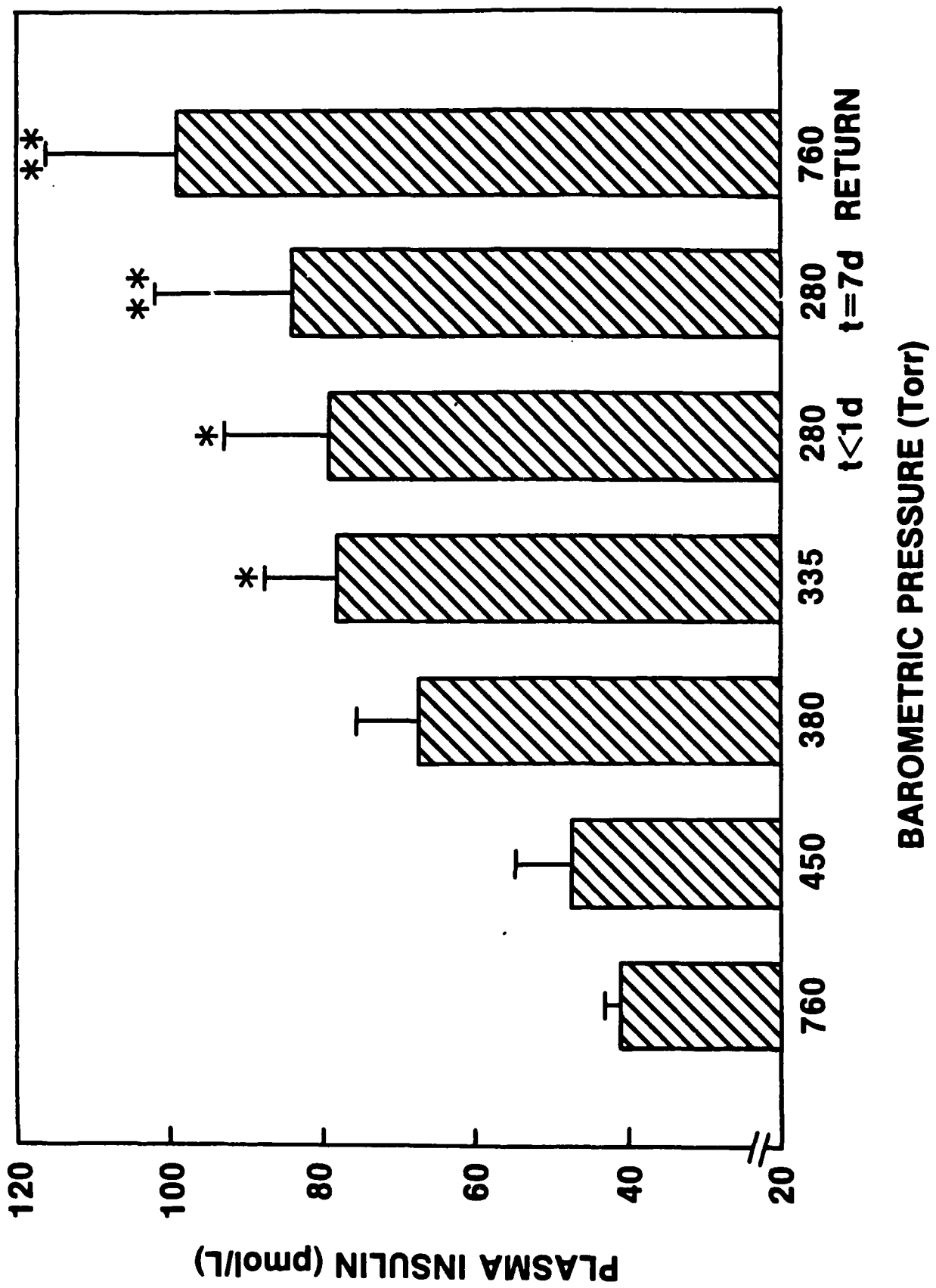
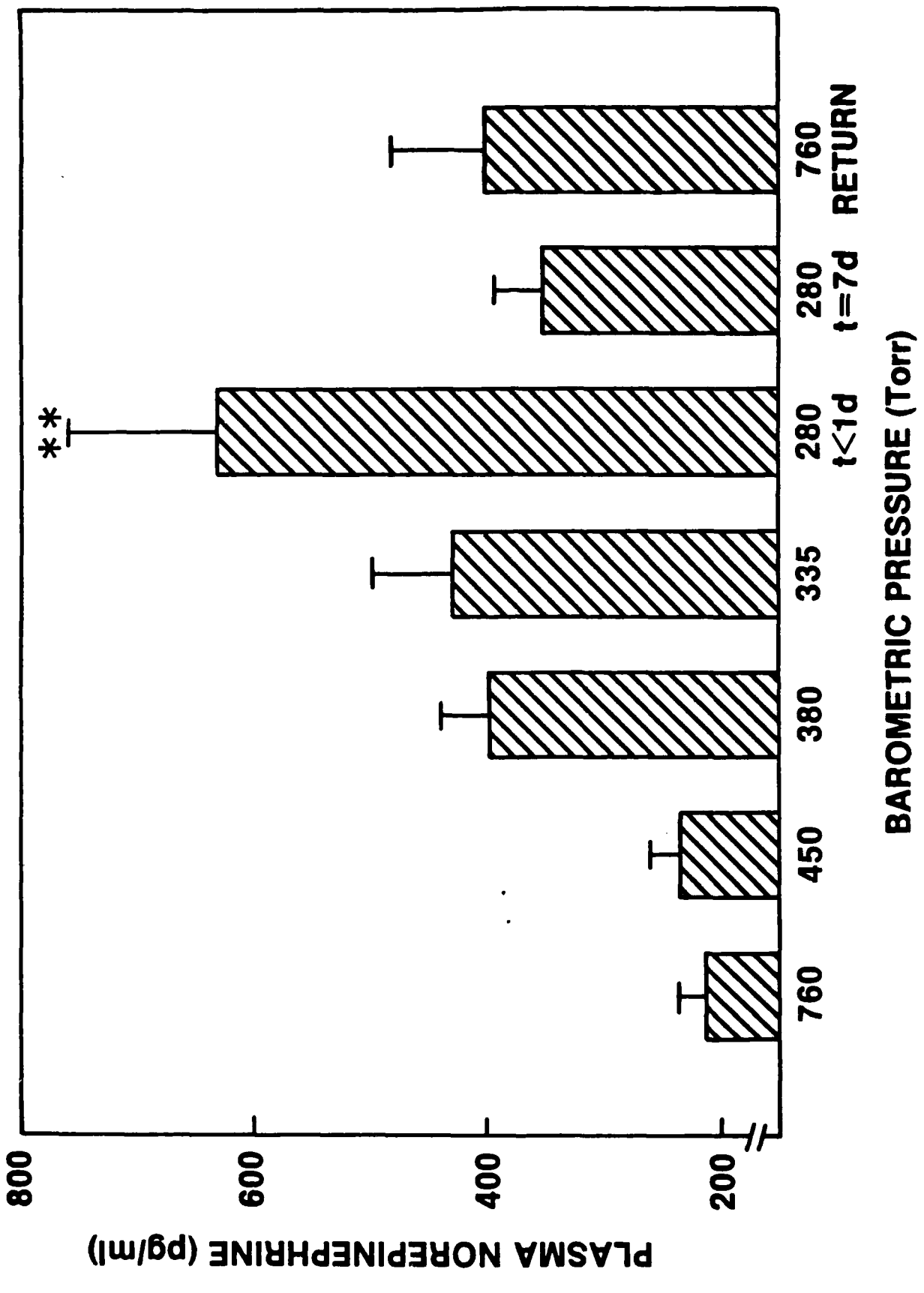

PLASMA INSULIN (pmol/L)
120
100
80
60
40
20
760
450
380
335
280
t<1d
280
t=7d
760
RETURN
BAROMETRIC PRESSURE (Torr)
*
*
*
**
**

FIGURE 4


PLASMA NOREPINEPHRINE (pg/ml)
800
600
400
200
**
760
450
380
335
280
280
760
BAROMETRIC PRESSURE (Torr)
t<1d
t=7d
RETURN